UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/635,370	08/09/2000	Kuanghui Lu	CIBT-P02-060	5518

28120 7590 04/18/2003

ROPES & GRAY
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER
LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
1636	21

DATE MAILED: 04/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/635,370	LU ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication app ars on the cover sheet with th correspondenc addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55,57-61,63-66,68,69 and 71-81* is/are pending in the application.

4a) Of the above claim(s) *1-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *55,57-61,63-66,68,69 and 71-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 August 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of a reply, filed February 6, 2003 as Paper No. 20, to the previous Office Action. Amendments were made to the claims. Specifically, new claims 79-81 were added.

Claims 1-55, 57-61, 63-66, 68, 69 and 71-81 are pending in the application. Claims 1-54 have been withdrawn as being drawn to non-elected inventions. Claims 55, 57-61, 63-66, 68, 69 and 71-81 are ready for examination in the instant application. Any rejection of record in the previous Office Action, Paper No. 17, mailed October 3, 2002, that is not addressed in this action has been withdrawn.

Information Disclosure Statement

The information disclosure statement filed October 1, 2002 has been considered, and a signed and initialed copy of PTO form 1449 is attached to this Office Action.

Drawings

New corrected drawings are required in this application because of the reasons set forth in the Draftspersons comments, which was attached to Office Action mailed July 30, 2001 as Paper No.10. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 55, 57-61, 63-66, 68, 69 and 71-81 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection not necessitated by amendment.**

Applicant claims any growth factor preparation that has the capacity to generate a population of non-adherent progenitor cells from pancreatic, liver or dermis tissue, wherein the population yields a substantially pure population of at least 75% purity. The claims read on a broad genus of growth factors that can give the very specific selection of a population of non-adherent progenitor cells with 75% purity. The claims also read on the ability to use any given growth factor preparation to generate a substantially pure population of non-adherent progenitor cells from a variety of different tissues (e.g., pancreatic, liver or dermis).

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case, the specification does not

sufficiently describe a representative number of growth factors for use with a specific tissue, by actual reduction to practice, to show the skilled artisan that they were in possession of the claimed invention.

Applicant claims the use of a growth factor preparation by function only, without any disclosed or known correlation between the elements and their function. The specification only provides teachings regarding the use of a single growth factor preparation, DCE (containing dexamethasone, cholera toxin and EGF) in order to obtain a substantially pure population of non-adherent progenitor cells from pancreatic tissue (see for example page 41, lines 26-36), wherein the purity is at least 75% pure. In fact the specification teaches that other growth factor preparations did not work as well as the DCE preparation in terms of giving a desirable yield (e.g., the 75% purity) that is claimed. The specification does not teach what other growth factor populations would give the specific selection of at least 75% purity for the population of non-adherent progenitor cells. In fact, the specification indicates that no other combination or individual growth factor preparation(s) gave a significant expansion of non-adherent progenitor cells (see for example page 41, lines 26-36), indicating that a composition that gives the claimed yield is rare. Furthermore, it is unclear that any growth factor preparation, or even the DCE growth factor preparation, will have the same desired yield when used in conjunction with other starting tissue besides pancreatic tissue (e.g., dermis or liver). For example, there is no art of record indicating that a progenitor cell obtained from a different tissue would have the same capability to respond to the factors in the DCE composition (e.g., are the same growth receptors present on the exemplified pancreatic cells also present on liver cells or dermal cells, or any tissue for that matter, such that they will respond in the same manner to the DCE composition,

thus yielding a substantially pure population of non-adherent progenitor cells of at least 75% purity?). Notably, the specification does not provide a basis as to why the DCE composition has the ability to produce a substantially pure population of non-adherent progenitor cells of at least 75% purity, therefore it is not possible for the skilled artisan to extrapolate from these findings to envision what other growth factors would have the same yield in non-adherent progenitor cells. Finally, it is unclear that the absence of a growth factor preparation, as indicated in claims 69 and 81, will give the desired yield of at least 75% purity for the same reasons set forth above. Therefore the skilled artisan cannot envision what other growth factor preparations can be used in the claimed method to achieve the desired selection of a population of non-adherent progenitor cells from pancreatic, liver or dermal tissue.

The prior art does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the prior art that allows one to envision a representative number of growth factor preparations that would give the desired selection of a population of progenitor cells that are at least 75% pure by disclosing the relevant features of the growth factor preparation so that one of skill in the art could envision such a preparation for a progenitor cell obtained from a particular tissue. Thus the skilled artisan cannot rely on the prior art to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application nor the prior art teaches a representative number of growth factor preparations that can be used to isolate a substantially pure population of non-adherent progenitor cells, wherein the selection calls for the isolation of a population that is at least 75% pure. As a result, the skilled artisan would not be able to envision

the claimed invention by relying on the teachings of the prior art or the instant specification. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

Claims 55, 57-61, 63-66, 68, 69 and 71-81 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), the most relevant of which are considered below:

Nature of the invention. The invention is a method of generating a substantially pure population of non-adherent progenitor cells from pancreatic, liver or dermal tissue, whereby the yield from the method is at least 75% pure. The invention calls for the use of any growth factor preparation in order to obtain these yields from multiple different tissue types (e.g., pancreatic, liver and dermis).

Scope of the invention. The scope of the invention is extremely broad, claiming the use of any growth factor preparation that will give the desired yield, a substantially pure population of non-

adherent progenitor cells (e.g., at least 75% pure, as per applicant's definition). The scope of the invention is further broadened by the fact that it is claimed that more than one type of starting tissue (e.g., pancreatic, liver or dermis) can be used with any growth factor preparation in order to obtain a substantially pure population of non-adherent progenitor cells, seemingly indicating that the type of growth factor preparation is irrelevant to obtaining the specific population of non-adherent progenitor cells. Additionally, several claims indicate that the growth factor preparation is not required in order to use the method to make the substantially pure population (i.e., claims 69 and 81).

State of the art. In a search of the prior art, there is no indication that the use of literally any growth factor preparation will have the same effect in terms of de-differentiating or isolating progenitor cells on all types of tissue. Similarly, the prior art shows no indication that the same growth factor preparation will have an equal effect on the generation of progenitor cells from different types of tissue (e.g., pancreatic and dermal tissue). It appears that the progenitor cells in the instant specification are not totipotent cells because the progenitor cells have not been shown as capable of differentiating into cell lineages that are different from the tissue from which the cells have been isolated (e.g., progenitor cells from pancreatic tissue lead to the generation of pancreatic cells, whether they be endocrine or exocrine). Therefore, the progenitor cells disclosed in the instant specification appear to have some level of differentiation, and will express different growth factor receptors that are responsive to different growth factors. As a result, the skilled artisan could not consult the prior art to identify which growth factor preparations would be useful for the isolation of a population of non-adherent progenitor cells

from different tissue types (e.g., pancreatic or liver tissue) and achieve the claimed substantial purity of at least 75%.

Number of working examples and Guidance provided by applicant. The specification provides guidance with regard to the use of the DCE growth factor preparation as it pertains to the isolation of an at least 75% pure population of non-adherent progenitor cells from pancreatic tissue (see for example page 41, lines 26-36). In particular, the specification indicates that only the specific DCE cocktail *significantly* enhanced the appearance of non-adherent progenitor cells (see for example page 41, lines 32-36), suggesting that this specific composition is necessary for the claimed yield. When consulting the disclosure for guidance, the skilled artisan would not be apprised of what other growth factor preparations would give the desired yield of the population of non-adherent progenitor cells. Furthermore, the skilled artisan would not be aware of how this particular cocktail would affect the production of a substantially pure population of non-adherent progenitor cells from liver or dermal tissue, as there is no disclosure of what growth factor preparations could be used in the claimed method. For example, different tissue types express distinct growth factor receptors (e.g., the receptors on dermal tissue would be different from those on pancreatic tissue), therefore there would be no way to extrapolate the use of one particular growth factor on different types of tissue without a significant level of unpredictability. As a result, the skilled artisan would not be able to consult the instant specification for guidance on how to make and use the invention along the full scope of the claims.

Level of skill in the art. The level of skill in the art is underdeveloped. There is no indication in either the prior art or in the instant specification that literally *any* growth factor preparation can be used to isolate a substantially pure population of non-adherent progenitor cells from

pancreatic, liver or dermis tissue at a level of at least 75% purity. The only indication is that the DCE preparation is capable of significantly enhancing the production of a substantially pure population of non-adherent progenitor cells from pancreatic tissue.

Unpredictability of the art and Amount of experimentation required. The art is highly unpredictable, owing to the limited disclosures in both the instant specification and the prior art, in conjunction with the broad scope of the claims and the level of skill in the art. The skilled artisan would not be able to make and use the invention as claimed because there is only an enabling disclosure for the use of one particular growth factor preparation that gives rise to a substantially pure population of non-adherent progenitor cells from pancreatic tissue wherein the enrichment of the progenitor cells is significantly increased (e.g., it gives the desired yield of at least 75%). In fact, as stated above, the specification indicates that only the DCE preparation was capable of giving such an increase in comparison to the other growth factor preparations. Furthermore, it is unclear how to extrapolate the use of this particular growth factor composition (or other growth factor compositions) to different tissues other than the exemplified pancreatic tissue (e.g., liver and dermal tissue), owing to the fact that other tissues express different receptors that respond to different growth factors; this lends itself to the overall unpredictability of the claimed invention. As a result, the skilled artisan would be forced to practice undue, unpredictable trial and error experimentation not only to identify what additional growth factor preparations would give the claimed yield as it related to the generation of non-adherent progenitor cells from pancreatic tissue, but also to identify what particular growth factor preparations would be useful for isolating the desired yields of non-adherent progenitor cells from liver or dermis tissue.

In conclusion, the invention as claimed is not enabled in light of the above Wands factor analysis. The scope of the invention is very broad in light of the teachings provided by the instant specification and the prior such that the skilled artisan would be required to practice undue and unpredictable trial and error experimentation in order to make and use the invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 77-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite the terminology "substantially pure", which is defined in the specification as being at least 75% pure (see for example page 18, lines 23-30). Claim 79 and 80, however, refer to substantially pure as being at least 50% or 60% pure, respectively. These claims are indefinite because it is unclear if the method calls for the isolation of a "substantially pure" population (being at least 75% pure as per applicant's definition), or a population with a purity of at least 50% purity. Furthermore, claim 81 refers to substantially pure as being at least about 100-fold enriched. In this instance, it is unclear what the nexus is between "substantially pure" and "about 100-fold enriched" because it is unclear from the definition in the specification as to whether or not 100-fold enriched is equivalent to at least 75% pure, thereby making the claim indefinite. **This is a new rejection not necessitated by amendment.**

Claims 69, 71-77 and 81 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: an explicit selection step whereby

the cell suspension is treated by a growth factor preparation thereby resulting in the production of a substantially pure population of non-adherent progenitor cells of at least 75% purity. This element is essential to the method whereby the growth factor preparation allows the expansion of the cell population such that a substantially pure population of at least 75% purity is obtained.

This is a new rejection not necessitated by amendment.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 55, 63-65, 69, 77 and 78 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1,3-5, 8, 15, 25 and 26 of U.S. Patent No. 6,326,201. **This rejection is maintained for the reasons set forth in the previous Office Action.**

Response to Arguments Concerning Rejections Under Double Patenting

Applicant responded to the previous double patenting rejection by indicating that a terminal disclaimer will be submitted along with an indication of allowable subject matter.

Applicant is advised that indication of allowable subject matter necessarily requires that the double patenting rejection be overcome, and the rejection will be maintained until the rejection is overcome either by submission of a terminal disclaimer or by an amendment to the claims that overcomes the double patenting rejection.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald D. Leffers Jr
PATENT EXAMINER
Gerald D. Leffers Jr
A.U. 1636

David A. Lambertson
April 16, 2003